

CLAIMS

1. A method of making a binding device comprising a first step of confining in the device a binding compound, the binding compound having affinity for a binding partner, a second step of preparing a plurality of affinity binders, each of said affinity binders comprising a first portion comprising the binding partner and a second portion adapted to bind selectively with a species, and thereafter a step of selecting at least one of the affinity binders and introducing said at least one affinity binder into the device so as to cause the binding partner to bind to the binding compound.
2. The method of claim 1 wherein the binding device is an extracorporeal device including means for connecting the device to a fluid source in a mammal.
3. The method of claim 1 or 2 wherein the binding device includes a semipermeable membrane for confining the binding compound.
4. The method of claim 1 or 2 wherein the binding compound is bound to a carrier.
5. The method of claim 4 wherein the carrier is selected from the group consisting of a wall of the device, a fixed matrix in the device, and a fill of beads or other granules.
6. The method of claim 1 or 2 wherein the second portions of the affinity binders are adapted to bind selectively with pathogenic species.
7. The method of claim 1 or 2 wherein the affinity binders comprise antibodies.
8. The method of claim 7 wherein the first portions of the affinity binders comprise Fc portions of the antibodies.
9. The method of claim 2 wherein the first portions of the affinity binders comprise avidin or biotin.
10. The method of claim 1 wherein the device is an extracorporeal treatment device, the device including means for removing blood from a mammal, passing at least a part of the blood through the device, and returning at least a part of the blood to the mammal.

11. The method of claim 1 or 2 wherein the binding compound comprises Protein A or Protein G.

12. The method of claim 2 or 10, including a step of administering to the mammal a targeting species bound to a targeted species, wherein the targeted species is selected from a Treatment Ligand and a Visualization Ligand.

13. The method of any of claims 2, 6 or 12, wherein the second portion of at least one affinity binder is adapted to bind selectively with a species comprising a targeting species bound to a targeted species.

14. The method of claim 12 or 13, including a step of extracorporeal adsorption of a species comprising a targeted species.

15. The method of any of claims 12, 13 or 14, including a step of extracorporeal adsorption of a species comprising a targeted species bound to a targeting species.

16. The method of any of claims 12-15 wherein the targeted species is a treatment ligand.

17. The method of claim 16, wherein the targeted species is an anti-cancer drug.

18. The method of claim 17 wherein the anti-cancer drug is selected from a radioactive molecule, a radioactive ion, a radioactive atom, a biological toxin, adriamycin, and calicheamicin.

19. The method of claim 10, wherein the targeted species is a visualization ligand.

20. The method of claim 19, wherein the visualization ligand, comprises a radioactive molecule, a radioactive ion, or a radioactive atom.

21. The method of any of claims 10-20 wherein the targeting species comprises somatostatin or an analog of somatostatin.

22. The method of any of claims 1-21, wherein at least one of the affinity binders comprises a first portion having affinity to the binding compound and a second portion having affinity to at least one of the group consisting of TNF alpha, IL-6, CD3+ DR+ T cells, CD4+CD28null T cells, CD3+, CD56+, DM1, VGO1, LAK1, CRP, INF gamma, CA, NAB, CA-NAB,

TGF β , P15E, Sialomucin, TH2 T cell epitope, tumor infiltrating lymphocyte (TIL) marker, lymphokine activated killer cell (LAK) marker, Interleukin 10 (IL-10), prostaglandin E2 (PGE2), mucin, suppressive E receptor (SER), immunosuppressive acidic protein (IAP), adhesion molecules, sR TNF alpha, sR TNF beta, sR IL-1, sR IL-2, sR IL-6, sR INF gamma, heat shock protein (HSP), antibodies to oxidized LDL (Ab-OxLDL), antibodies to HSP, CRP, triglycerides, IL-2, metalloproteinases, other proteinases, fibrinogen, creatine kinase, IL-I -Beta, IL-I-Ra, PDGF, angiotensin II, MCSF, pregnancy associated plasma protein A (PAPPA), antibodies specific to any of the following: the β 1 adrenergic receptor, ADP-ATP carrier, alpha cardiac myosin heavy chain isoform, beta cardiac myosin heavy chain isoform, G Protein coupled receptors, and heart mitochondria, oxidants, and toxins selected from the group consisting of botulinum toxin, tetanus toxin, ricin toxin, and ricin A peptide toxin, sulfur mustard, prescription drugs, over-the-counter drugs, drugs of abuse, chemical poisons, and toxic metabolites thereof.

23. The method of claim 18, wherein the second portion has affinity to ricin A peptide.

24. The method of any of claims 12-23, wherein the targeted species is incorporated in a liposome.

25. The method of any of claims 12-24, wherein the targeting species has affinity for a tumor cell.

26. The method of claim 25, wherein the tumor is a cancer selected from ovarian cancer, prostate cancer, and colon cancer.

27. The method of claims 25 or 26 wherein the target binding site on the tumor cell is selected from: CEA, p97 epitope, CD33 antigen epitope, somatostatin receptor, p 53, Her-2neu, PSMA, and CA-125.

28. The method of claim 10 or 22, including a step of administering to the mammal a drug selected from a receptor antagonist and an anti-inflammatory cytokine.

29. The method of claim 10 or 22, wherein the device is an extracorporeal treatment device, the device being used for treatment of a mammal for a disease state selected from: cancer, atherosclerosis (AS),

coronary artery disease (CAD), peripheral atherosclerotic vascular disease (PASVD), atherosclerotic cerebro vascular disease (ASCVD), acute ischemic syndromes, acute myocardial infarction (MI) and unstable angina (UA), inflammatory diseases, idiopathic dilated cardiac myopathy (IDCM),
5 autoimmune disease, sepsis, infectious disease, diseases associated with exotoxins, diseases associated with endotoxins, autoimmune-associated vascular diseases, rheumatoid arthritis, drug overdose, drug intoxication, and poisoning with a chemical poison.

30. The method of any of claims 1 to 29, wherein the extracorporeal
10 binding device comprises regeneration means, for regenerating the second portion of at least one affinity binder.

31. The method of claim 30, wherein the regeneration means comprise a solution.

32. The method of claim 31, wherein the solution comprises an acidic
15 buffer.

33. In combination, a device having contained therein a binding compound bound to a carrier, the binding compound having affinity for a binding partner, and a plurality of affinity binders, each of said affinity binders comprising a first portion comprising the binding partner and a second portion
20 adapted to bind selectively with a species, the second portions of each of said affinity binders differing from each other.

34. The combination of claim 33 wherein the device is an extracorporeal device including means for connecting the device to a fluid source in a mammal.

25 35. The combination of claim 33 or 34, wherein at least one of the affinity binders comprises a first portion having affinity to the binding compound and a second portion having affinity to at least one of the group consisting of TNF alpha, IL-6, CD3+ DR+ T cells, CD4+CD28null T cells, CD3+, CD56+, DM1, VGO1, LAK1, CRP, INF gamma, CA, NAB, CA-NAB,
30 TGF β , P15E, Sialomucin, TH2 T cell epitope, tumor infiltrating lymphocyte (TIL) marker, lymphokine activated killer cell (LAK) marker, Interleukin 10 (IL-10), prostaglandin E2 (PGE2), mucin, suppressive E receptor (SER),

immunosuppressive acidic protein (IAP), adhesion molecules, sR TNF alpha, sR TNF beta, sR IL-1, sR IL-2, sR IL-6, sR INF gamma, heat shock protein (HSP), antibodies to oxidized LDL (Ab-OxLDL), antibodies to HSP, CRP, triglycerides, IL-2, metalloproteinases, other proteinases, fibrinogen, creatine kinase, IL-1 -Beta, IL-1-Ra, PDGF, angiotensin II, MCSF, pregnancy associated plasma protein A (PAPPA), antibodies specific to any of the following: the β 1 adrenergic receptor, ADP-ATP carrier, alpha cardiac myosin heavy chain isoform, beta cardiac myosin heavy chain isoform, G Protein coupled receptors, and heart mitochondria, oxidants, and toxins selected from the group consisting of botulinum toxin, tetanus toxin, ricin toxin, and ricin A peptide toxin, sulfur mustard, prescription drugs, over-the-counter drugs, drugs of abuse, chemical poisons, and toxic metabolites thereof.

36. The combination of any of claims 33-35, wherein the device comprises regeneration means for regenerating the second portion of at least one affinity binder.

37. The combination of claim 36, wherein the regeneration means comprise a solution.

38. The combination of claim 37, wherein the solution is an acidic buffer.

39. The combination of any of claims 33, 34, or 36-38 wherein at least one of the affinity binders comprises a second portion having affinity to a targeted species bound to a targeting species.

40. The combination of claim 39 wherein the targeted species comprises a radioactive molecule, a radioactive atom, or a radioactive ion.

41. A reagent comprising an immunogenic preparation of a molecular inflammatory factor (MIF).

42. A method of treating atherosclerosis, comprising administering to a mammal in need of such treatment the reagent of claim 41.

43. An extracorporeal device, comprising at least one affinity adsorbent, said affinity adsorbent binding a chemical species selected from the group consisting of exotoxins and endotoxins.

44. The device of claim 43 wherein the affinity adsorbent binds the species specifically.

45. The device of claim 43 or 44 wherein the affinity adsorbent is chemically bound to a matrix in said device.

5 46. The device of any of claims 43-45 wherein the device comprises at least two affinity adsorbents, said affinity adsorbents binding selectively to two different exotoxins, two different endotoxins, or an endotoxin and an exotoxin.

47. The device of claims 41-43, wherein the affinity adsorbent is selected from antibodies, antibody fragments, synthetic antibody binding site
10 analogs, genetically engineered synthetic antibody binding site analogs, exotoxin or endotoxin receptor binding sites, synthetic or genetically engineered exotoxin or endotoxin receptor binding site analogs.

48. The device of any of claims 43-47 further comprising means for regenerating at least one affinity adsorbent.

15 49. The device of claim 48 wherein the regeneration means comprise a solution.

50. The device of claim 49, wherein the solution comprises a buffer.

51. The device of claim 50 wherein the buffer is an acidic buffer.

52. A method of removing a species from a mammal comprising
20 introducing into the mammal an affinity binder which selectively binds the species, the affinity binder including a binding partner portion having affinity for a binding compound, and thereafter removing the affinity binder by capturing the affinity binder in a device having contained therein the binding compound, wherein the species is selected from the group consisting of TNF
25 alpha, IL-6, CD3+ DR+ T cells, CD4+CD28null T cells, CD3+, CD56+, DM1, VGO1, LAK1, CRP, INF gamma, CA, NAB, CA-NAB, TGF β , P15E, Sialomucin, TH2 T cell epitope, tumor infiltrating lymphocyte (TIL) marker, lymphokine activated killer cell (LAK) marker, Interleukin 10 (IL-10), prostaglandin E2 (PGE2), mucin, suppressive E receptor (SER),
30 immunosuppressive acidic protein (IAP), adhesion molecules, sR TNF alpha, sR TNF beta, sR IL-1, sR IL-2, sR IL-6, sR INF gamma, heat shock protein (HSP), antibodies to oxidized LDL (Ab-OxLDL), antibodies to HSP, CRP,

triglycerides, IL-2, metalloproteinases, other proteinases, fibrinogen, creatine kinase, IL-I -Beta, IL-I-Ra, PDGF, angiotensin II, MCSF, pregnancy associated plasma protein A (PAPPA), antibodies specific to any of the following: the β 1 adrenergic receptor, ADP-ATP carrier, alpha cardiac myosin heavy chain isoform, beta cardiac myosin heavy chain isoform, G Protein coupled receptors, and heart mitochondria, a targeted species bound to a targeting species, and toxins selected from the group consisting of botulinum toxin, tetanus toxin, ricin toxin, ricin A peptide toxin, sulfur mustard, prescription drugs, over-the-counter drugs, drugs of abuse, chemical poisons, and toxic metabolites thereof.

53. A species-removing device having contained therein a binding compound attached to a matrix and an affinity binder bound by affinity binding to the binding compound, the affinity binder having affinity for a species selected from the group consisting of TNF alpha, IL-6, CD3+ DR+ T cells, CD4+CD28null T cells, CD3+, CD56+, DM1, VGO1, LAK1, CRP, INF gamma, CA, NAB, CA-NAB, TGF β , P15E, Sialomucin, TH2 T cell epitope, tumor infiltrating lymphocyte (TIL) marker, lymphokine activated killer cell (LAK) marker, Interleukin 10 (IL-10), prostaglandin E2 (PGE2), mucin, suppressive E receptor (SER), immunosuppressive acidic protein (IAP), adhesion molecules, sR TNF alpha, sR TNF beta, sR IL-1, sR IL-2, sR IL-6, sR INF gamma, heat shock protein (HSP), antibodies to oxidized LDL (Ab-OxLDL), antibodies to HSP, CRP, triglycerides, IL-2, metalloproteinases, other proteinases, fibrinogen, creatine kinase, IL-I -Beta, IL-I-Ra, PDGF, angiotensin II, MCSF, pregnancy associated plasma protein A (PAPPA), antibodies specific to any of the following: the β 1 adrenergic receptor, ADP-ATP carrier, alpha cardiac myosin heavy chain isoform, beta cardiac myosin heavy chain isoform, G Protein coupled receptors, and heart mitochondria, a targeted species bound to a targeting species, and toxins selected from the group consisting of botulinum toxin, tetanus toxin, ricin toxin, ricin A peptide toxin, sulfur mustard, prescription drugs, over-the-counter drugs, drugs of abuse, chemical poisons, and toxic metabolites thereof.

54. The species-binding device of claim 53 wherein the affinity binder comprises an antibody, an antibody fragment, a synthetic antibody fragment, a synthetic antibody binding site, and a synthetic antibody binding site analog.

55. The species-binding device of claim 53 or 54 wherein one of the
5 binding compound and the affinity binder comprises Avidin, and the other of the binding compound and the affinity binder is biotinylated.